

# TUNING THE SP TO FM TRANSITION OF COBALT NANOPARTICLES IN VIEW OF BIOMEDICAL APPLICATIONS

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Magnetic nanoparticles are a powerful and versatile diagnostic tool in biology and medicine. Bound to a suitable antibody, they are used to label specific molecules, structures or microorganisms. Established techniques such as magnetic cell separation use magnetic field gradients to manipulate and isolate magnetically labeled cells. More recently, magnetic immunoassay techniques have been developed in which the magnetic field generated by the magnetically labeled targets is detected directly with a sensitive magnetometer. In addition, drug delivery and contrast enhancement in MRI would benefit from a simple reproducible chemical synthesis of monodispersed magnetic nanoparticles.

In general, the use of magnetic particles for biological and medical applications has been intense and focused on iron oxides.

At the present point, development of better techniques would require better controlled nanoparticles. Two possible approaches are either improving synthesis of the iron oxide nanoparticles or changing the magnetic material. Synthesis of iron oxides often shows low reproducibility (due to the complex oxygen chemistry), polycrystallinity and low control. T. Hyeon *et al.* [1] recently showed the synthesis of monodisperse Fe<sub>2</sub>O<sub>3</sub> nanoparticles. Even if the results are remarkable, still, Fe<sub>2</sub>O<sub>3</sub> is a weak ferrimagnetic material, while Co (and Fe and Ni and their alloys) is ferromagnetic and has shown an outstanding capacity of shape control, perhaps thanks to the particular epsilon crystal structure which is more complex than the conventional hexagonal and cubic compact faces and allows better shape control [2], while keeping the magnetic properties almost unchanged.

The magnetic transition from the superparamagnetic (SP) to ferromagnetic (FM) state as the magnetic susceptibility and coercivity is determined at the synthesis. Depending on the desired properties, different magnetic behavior is requested. For example, Chemla *et al.* [3] recently showed a method for a ultra high sensitive immunoassays where monodisperse SP nanoparticles are needed. Many tests reveal the presence of a molecule or disease causing organism by detecting the binding of an antibody to the target. When antibodies labeled with magnetic nanoparticles binds to the target on a

surface, brief exposure to a magnetic field causes these probes collectively to give off a strong magnetic signal. Meanwhile unbound antibodies tumble about in all directions producing no net signal. For a 20 nm Fe<sub>2</sub>O<sub>3</sub> particle, Neel relaxation (bound particles) is about 1 s while Brownian relaxation (unbound particles) is about 1 μs [3]. This last property makes it possible to read the results without first washing away any probes that fail to find their target.

Besides, weakly FM particles capable of self assembly in solution would be useful for dynamically change the local concentration of molecules linked (conjugated) to the nanoparticles surface.

The general requirements would often be of magnetic particles displaying a large magnetic susceptibility, while keeping interparticle interactions low so they do not agglomerate

Progress has been made recently by Riffle and Rutnakornpituk (micelle-grown cobalt nanoparticles of 10 nm diameter). Other groups have also developed magnetic nanocrystal synthesis [4]. In this paper we present the synthesis of monodisperse cobalt ferrofluids with controlled size and shape. The synthesis is carried out in non polar solvents, necessary for the size and shape control. Recent developments in the solubilization of this nanoparticles in aqueous solutions are commented.

By modifying the volume or the shape, and therefore the shape anisotropy, the SP to FM transition can be modified. In addition, by partially oxidizing the particles, coercivity may be increased (for passive sensor purposes) thanks to the exchange between the CoO and the Co. Surface chemistry, like absorption of CO may also modify magnetic properties.

The particles are obtained by rapid pyrolysis of Co carbonyl in dichlorobenzene in presence (about 1%) of surfactants (carboxylic acids, phosphonic acids and amines), which: control the crystal growth, therefore the size and the shape of the particles, solubilize the particles, avoids agglomeration and passivates them (but do not fully prevent) against oxidation. In the presence of oleic acid and trioctyl phosphine oxide, spherical monodisperse particles are obtained (Fig.1).

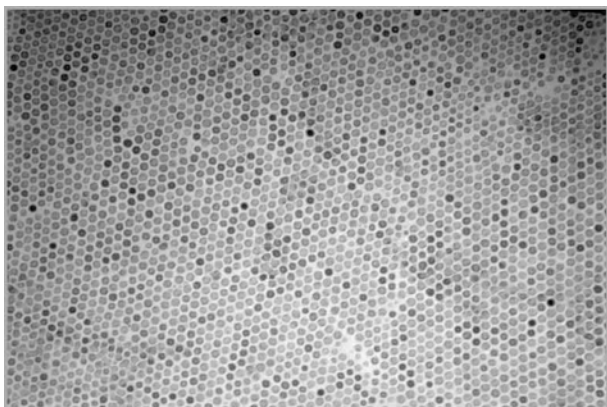


Fig.1. TEM picture of 10 nm Co nanoparticles

A concentrated solution of  $\text{Co}_2(\text{CO})_8$  (0.40 to 0.80 g in 2-3 ml of o-dichlorobenzene anhydrous) was injected in an o-dichlorobenzene anhydrous refluxing bath (15 ml,  $T=181^\circ\text{C}$ ). All reactions were carried under Ar following standard airless procedures using commercially available pure reactants. Macroscopic amounts ( $10^{16}$  particles/ml) of monodispersed nanoparticles were thus obtained. The decomposition and nucleation occurs instantaneously upon injection. The lifetime of atoms in solution is short leading to the simultaneous formation of many small metal clusters (nuclei). Control of the bath temperature and the surfactant composition modifies the strength of the metallic particle-organic molecule bonding. Thus, by controlling the precursor to surfactant ratio, the reaction temperature and injection time, the size of the spherical particles can be controlled and varied between 3 to 16 nm (Fig.2).

Small magnetic particles are single domain, i.e., all the atomic magnetic spins of the particle are coupled in the same direction and the particle behaves as a single magnetic dipole. Depending on anisotropy, size and temperature, the magnetic dipole of the particles will be free to rotate (superparamagnetism) or will be blocked in the anisotropy direction (ferromagnetism). In the first case, the time average of the magnetic moment of the particle is zero. The relation between anisotropy energy and thermal energy is  $KV=k_B T$  (where  $K$  is the anisotropy constant,  $V$  the particle volume,  $k_B$  the boltzman constant and  $T$  the temperature), determines the transition between the SP and the FM regime. Once the particles become FM, magnetic interactions among them start to play a crucial role following the relation between magnetic interaction and thermal energy  $2\mu^2/a^3 = k_B T$  (where  $\mu$  is the magnetic dipole moment and  $a$  is the particle diameter,  $k_B$  the boltzman constant and  $T$  the temperature).

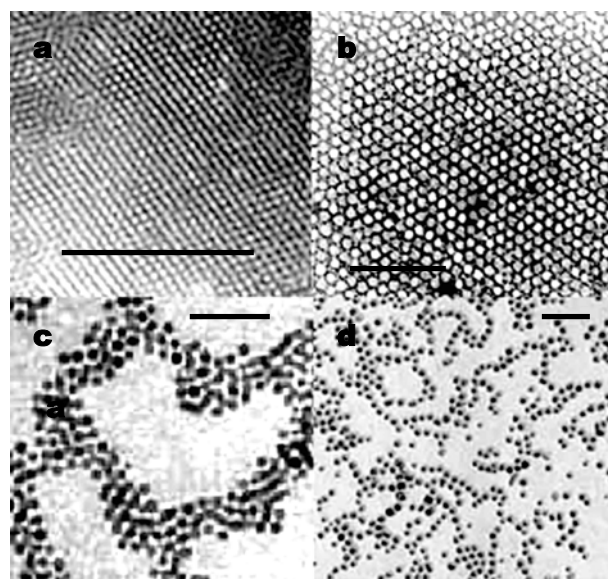
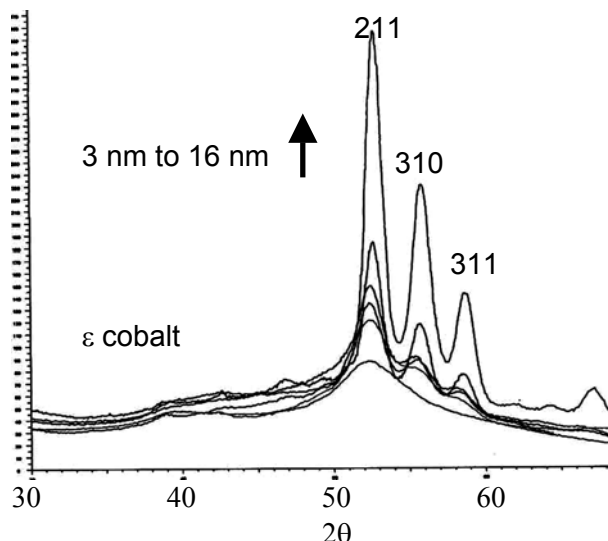
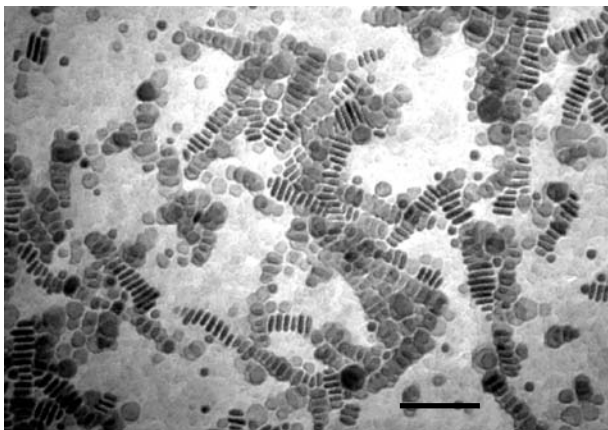


Fig.2. XRD and TEM as a function of particle size. The XRD peaks increases in intensity and become narrower as the size of the crystal domain increase. All bar are 100 nm.

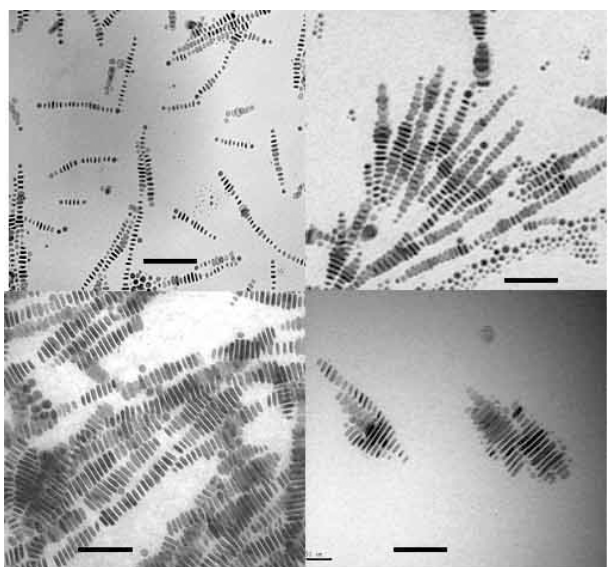
Thus, due to strong dipole-dipole interactions, large nanocrystals form closed loops in order to minimize the magnetostatic energy (Fig.2d). In the transition range, a mixture of hexagonal monolayer and closed loops is observed (Fig.2c) suggesting that in this case, the SP-FM transition is taking place at room temperature for particles with sizes around 12 nm, as supported by low susceptibility magnetization measurements (not shown).

In addition to the volume, the shape may be modified to obtain objects with anisotropies up to an order of magnitude higher than the crystal anisotropy, shifting considerably the SP to FM transition to lower temperatures for a constant particle volume.



*Fig.3 TEM picture of Co nanodisks shaped crystals. Bar is 100 nm*

By mixing small amounts of amines to the surfactant mixture, Co nanodisks have been synthesized (Fig.3). And as previously, the diameter may be modified (Fig.4). These crystals show a strong anisotropy and spontaneously self-assemble into large ribbons. Thus, when these particles are introduced in solution, they will find each other, and so any molecule that is attached to them.



*Fig.4. Co nanodisks of different average diameters. Bars are 100 nm.*

It can be easily argued the interest of having particles that interact strongly between them or with an external field, but not so much that they collapse and precipitate. In addition of large SP particles which give a large signal without interacting.

As an example of tuning the magnetic properties, small disk-shaped particles will show a FM behavior for much smaller magnetic moments than the corresponding spheres, thus they will have a

weak tendency for self assembly so they may be easily redispersed (by agitation, sonication or soft T increase) and once they are far apart one from the other, the re-call interactions will be small, and independent tests may be performed before letting them slowly self assemble again. Assemblies of large disks will attach strongly and may be easily collectively transported by an external field. Large spherical particles may be useful for cell separation and drug delivery as small ones may be useful for ultra fast detection and labeling.

Proof of the quality and magnetic character of the samples yielded by this approach comes from observations of the spontaneous self-assembly of the nanocrystals, as well as from the formation of unique superstructures, such as chains and ribbons of disks. All sizes and shapes self-assemble into superstructures as a colloidal solution is allowed to evaporate slowly in a controlled atmosphere. A drop of the colloids (2% weight of particles) was put onto a carbon-coated TEM grid at room temperature and slowly evaporated (in a covered watch glass). The use of high boiling solvents (like o-dichlorobenzene), allows slow evaporation at RT, which permits the particles to diffuse to their lowest energy sites during evaporation, producing well-defined super-structures. The final arrangement of the nanocrystal assembly is driven by the balance of surface tension, van der Waals forces, and magnetic interactions among SP or FM particles.

Spherical particles self-assemble into hexagonal 2D superlattices (Fig.1). This assembly is determined by the size of the crystals and the thickness of the coating layer ( $\sim 2$  nm). Higher initial concentrations lead to 3D self-assemblies where the particles in the second layer occupy sites determined by the hexagonal arrangements.

As the particle diameter is increased, the magnetic moment increases and thus interparticle interactions. For 12 nm SP particles, their large moment leads to strong repulsive interactions that help to order the solid particles as the sample is dried into the microscope grid. Thus, the largest and more ordered self assemblies are found for the larger SP particles. However, when the volume further increases, particles become FM at room temperature and start forming chains as previously commented.

In addition, particles oxidize progressively inwards when  $O_2$  is bubbled through the solution. By controlling the oxygen rate, the thickness of the CoO layer may be determined. CoO is antiferromagnetic and Co is FM. It has been repeatedly observed that as adjacent layers of FM and AFM material, CoO-Co core-shell structures display an increase in coercivity (memory) and a

shift of the hysteresis loop after cooling the sample under applied field due to exchange interactions. This parameter may also be used to finely tune the properties of the desired particles.

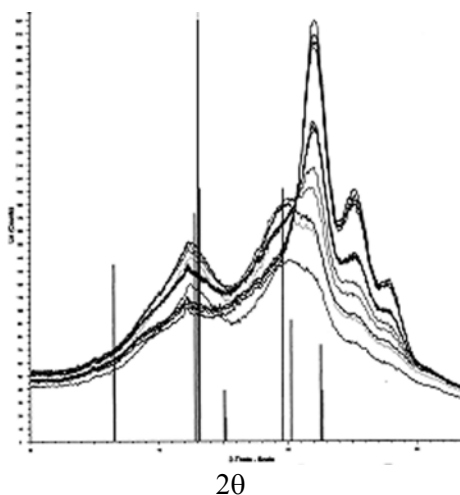


Fig.5 XRD of a progressive Co nanoparticle oxidation. Vertical lines correspond to CoO peaks.

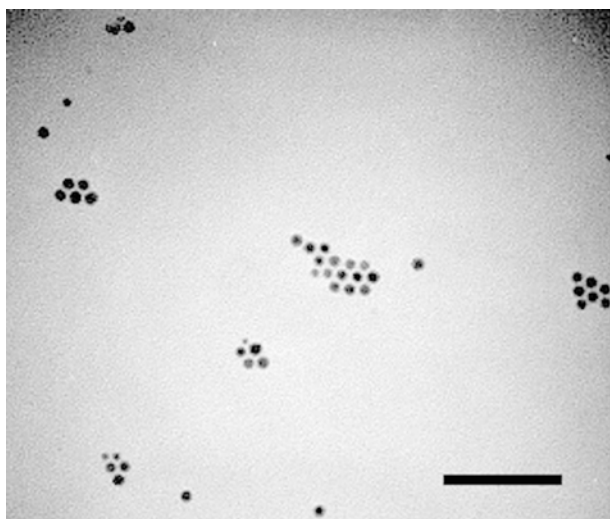


Fig.6 TEM of CoO-Co particles. CoO appears as a lighter ring around a dark core (due to electron density differences).

These particles are completely insoluble in water and, moreover, they are attacked and rapidly transformed into  $\text{Co}(\text{OH})_2$ . There is an intense effort of solubilizing such particles into aqueous solutions for developing biomedical techniques. Up to now there are four main approaches: i) growing epitaxially another metallic shell which will protect the particle and make it soluble (as Au or Pt), ii) wrapping the particles with a polymer consisting of hydrophobic and hydrophilic sections, iii) growing amorphous silica around the particle and, iv) attaching a surfactant molecule, like sugars, that makes the particle water soluble.

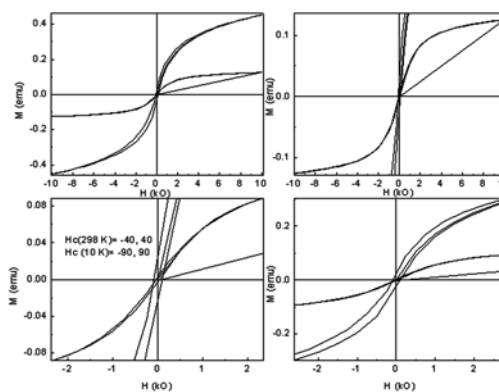


Fig.7. Hysteresis loop at low  $T$  after field cooling at 1 Tesla showing an increase of the coercivity and shift in the x-axis for samples which have been oxidized (by bubbling  $\text{O}_2$  into the solution).

In conclusion, promising results in nanocrystal synthesis may help the development of magnetic nanosensors and nanoactuators, first *in vitro* and then *in vivo*, for all the existing techniques applying magnetic carriers and new to come.

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**ACKNOWLEDGEMENTS:** This work was supported by the NIH National Center for Research Resources, Grant Number 1 R01 RR-14891-01 through the U.S. Department of Energy under Contract No. DE-AC03-76SF00098.